

Amendments to the Claims:

The following listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method for detecting multiple sclerosis (MS) or a condition associated with multiple sclerosis, ~~superantigen activity~~ in a biological sample, characterized in that wherein a superantigen activity is detected, said superantigen activity being induced by the expression product of the *env* gene of MSRV-1 comprising the sequence referenced in SEQ ID NO: 1, or a variant thereof having at least 90% sequence identity with SEQ ID NO: 1, or a fragment of SEQ ID NO: 1, said method comprising:
detecting an amount of lymphocytes bearing a V β 16 and/or V β 17 determinant in said biological sample; and
calculating an amount of expansion or loss of lymphocytes bearing a V β 16 and/or V β 17 determinant based on said detected amount,
wherein a majority expansion of lymphocytes bearing a V β 16 and/or V β 17 determinant or a majority loss of lymphocytes bearing a V β 16 and/or V β 17 determinant is demonstrated indicates the superantigen activity.
2. (Currently Amended) The detection method as claimed in claim 1, ~~characterized in that~~wherein a majority expansion of lymphocytes bearing a V β 16 determinant is demonstrated.
3. (Currently Amended) The detection method as claimed in claim 1, ~~characterized in that~~wherein a majority loss of lymphocytes bearing a V β 16 determinant is demonstrated.
4. (Currently Amended) The method as claimed in claim 2, ~~characterized in that~~wherein a majority expansion of lymphocytes bearing a V β 16 determinant and a co-expansion of lymphocytes bearing V β s chosen from at least any one of V β 2, V β 3, V β 7, V β 8, V β 12, V β 14, V β 17 and V β 22 are demonstrated.

5. (Currently Amended) The method as claimed in claim 3, ~~characterized in that~~wherein a majority loss of lymphocytes bearing a V β 16 determinant and a co-decrease of lymphocytes bearing V β s chosen from at least any one of V β 2, V β 3, V β 7, V β 8, V β 12, V β 14, V β 17 and V β 22 are demonstrated.

6. (Currently Amended) The method as claimed in claim 1, ~~characterized in that~~wherein the biological sample originates from a patient suffering from ~~an autoimmune disease~~ multiple sclerosis.

7. (Currently Amended) The method ~~for detecting superantigen activity~~ as claimed in claim 1, ~~characterized in that~~wherein:

(i) a culture supernatant of blood mononucleated cells or of choroid plexus cells or of leptomeningeal cells, said cells originating from patients suffering from ~~an autoimmune disease or suspected of having a risk of developing the disease~~ multiple sclerosis or of an established cell line, is sampled, and

(ii) said culture supernatant, or a part of the culture supernatant is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, and

(iii) said expansion and, optionally, a co-expansion, or said loss and, optionally, co-decrease, of the blood mononucleated cells of step (ii) are detected.

8. (Currently Amended) The method as claimed in claim 7, ~~characterized in that~~wherein the blood mononucleated cells originating from patients ~~originate from patients~~ suffering from multiple sclerosis (~~MS~~) and are chosen from monocytes and B lymphocytes and the blood mononucleated cells originating from healthy donors are chosen from T lymphocytes.

9. (Currently Amended) The method ~~for detecting superantigen activity~~ as claimed in claim 1, ~~characterized in that~~wherein:

(i) blood mononucleated cells are sampled, said cells originating from patients suffering from ~~an autoimmune disease or from patients suspected of having a risk of developing an autoimmune disease~~, multiple sclerosis and from healthy individuals,

(ii) said blood mononucleated cells originating from patients or from healthy individuals are brought into contact with culture supernatants, or a fraction of culture supernatant, of cells chosen from blood mononucleated cells, choroid plexus cells and leptomeningeal cells, and cells derived from established cell lines, and

(iii) said expansion and, optionally, co-expansion, or said loss and, optionally, co-decrease, using the blood mononucleated cells of step (i) are detected.

10. (Currently Amended) The method as claimed in claim 7, ~~characterized in that~~wherein said expansion and, optionally, co-expansion is demonstrated using ligands, each ligand being specific for a determinant chosen from V β 16, V β 2, V β 3, V β 7, V β 8, V β 12, V β 14, V β 17 and V β 22, and in that said loss and, optionally, co-decrease is demonstrated using ligands, each ligand being specific for a determinant chosen from V β 16, V β 2, V β 3, V β 7, V β 8, V β 12, V β 14, V β 17 and V β 22.

11. (Currently Amended) The method as claimed in claim 10, ~~characterized in that~~wherein the ligand is an antibody or antibody fragment.

12. (Currently Amended) The method as claimed in claim 7, ~~characterized in that~~wherein, in order to demonstrate said expansion and, optionally, co-expansion or said loss and, optionally, co-decrease, the following is carried ~~out~~out:

(i) extraction of the total RNAs from the blood mononucleated cells which have been placed together with MS culture supernatant or a fraction of MS culture supernatant and together with control culture supernatant or a fraction of control culture supernatant,

(ii) reverse transcription of said RNAs,

(iii) amplification specific for each V β family using a given pair of primers,

(iv) labeling of the amplification products obtained, with any suitable label,
(v) electrophoresis of said amplification products and analysis of the
electrophoretic profiles obtained, using a suitable detector.

13. (Currently Amended) The method as claimed in claim 12, ~~characterized in that~~
wherein the blood mononucleated cells originating from patients ~~originate from patients~~
suffering from MS ~~and~~ are chosen from lymphocytes.

14-20. (Canceled)

21. (Currently Amended) The method as claimed in ~~claim 19~~ claim 1, ~~characterized~~
~~in that~~ wherein the superantigen activity is induced by the envelope protein of MSRV-1
referenced in SEQ ID No. ~~NO: 2~~ or by a fragment of said protein.

22. (Currently Amended) The method as claimed in ~~claim 19~~ claim 1, ~~characterized~~
~~in that~~ wherein the superantigen activity is induced by the *env* gene of MSRV-1 referenced in
SEQ ID No. ~~NO: 1~~ or a fragment of said gene.

23-31. (Canceled)

32. (Currently Amended) A method for detecting ~~superantigen activity in a~~
~~biological sample, from patients suffering from multiple sclerosis characterized in that multiple~~
~~sclerosis (MS) or a condition associated with multiple sclerosis, wherein a superantigen activity~~
~~is detected, said superantigen activity being induced by the expression product of the env gene~~
~~of MSRV-1 comprising the sequence referenced in SEQ ID NO: 1, or a variant thereof having at~~
~~least 90% sequence identity with SEQ ID NO: 1, or a fragment of SEQ ID NO: 1, said method~~
~~comprising:~~

detecting an amount of lymphocytes bearing a V β 7 determinant in said
biological sample; and

calculating an amount of expansion or loss of lymphocytes bearing a V β 7
determinant based on said detected amount,

wherein a majority expansion of lymphocytes bearing a V β 7 determinant or a majority loss of lymphocytes bearing a V β 7 determinant ~~is demonstrated~~ indicates the superantigen activity.

33. (Currently Amended) The method as claimed in claim 32, ~~characterized in that:~~ wherein:

(i) a culture supernatant of blood mononucleated cells or of choroid plexus cells or of leptomeningeal cells, said cells originating from patients suffering from ~~an autoimmune disease or suspected of having a risk of developing the disease~~ multiple sclerosis or of an established cell line, is sampled, and

(ii) said culture supernatant, or a part of the culture supernatant is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, and

(iii) said expansion and, optionally, a co-expansion, or said loss and, optionally, co-decrease, of the blood mononucleated cells of step (ii) are detected.

34. (Currently Amended) The method as claimed in claim 33, ~~characterized in that~~ wherein the blood mononucleated cells originating from patients ~~originate from patients~~ suffering from MS ~~and~~ are chosen from B lymphocytes and monocytes and the blood mononucleated cells originating from healthy donors are chosen from T lymphocytes.

35. (Currently Amended) The method as claimed in claim 32, ~~characterized in that:~~ wherein:

(i) blood mononucleated cells are sampled, said cells originating from patients suffering from ~~an autoimmune disease or from patients suspected of having a risk of developing an autoimmune disease,~~ multiple sclerosis and from healthy individuals,

(ii) said blood mononucleated cells originating from patients or from healthy individuals are brought into contact with culture supernatants, or a fraction of culture

supernatant, of cells chosen from blood mononucleated cells, choroid plexus cells and leptomeningeal cells, and cells derived from established cell lines, and

(iii) said expansion and, optionally, co-expansion, or said loss and, optionally, co-decrease, using the blood mononucleated cells of step (i) are detected.

36. (Currently Amended) The method as claimed in claim 32, ~~characterized in that:~~wherein:

(i) a culture supernatant of blood mononucleated cells or of choroid plexus cells or of leptomeningeal cells, said cells originating from patients suffering from ~~an autoimmune disease or suspected of having a risk of developing the disease~~ multiple sclerosis or of an established cell line, is sampled, and

(ii) said culture supernatant, or a part of the culture supernatant is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, and

(iii) said expansion and, optionally, a co-expansion, or said loss and, optionally, co-decrease, of the blood mononucleated cells of step (ii) are detected using a ligand or amplification combined with electrophoresis.

37. (Currently Amended) The method ~~for detecting superantigen activity as claimed in claim 1, characterized in that:~~wherein:

(i) a polypeptide as identified by SEQ ID ~~No.~~NO: 2, or a fragment of said polypeptide, is produced or synthesized, said fragment being at least six amino acids in length,

(ii) said polypeptide is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, and

(iii) said expansion and, optionally, a co-expansion, or said loss and, optionally, co-decrease, of the blood mononucleated cells of step (ii) are detected.

38. (Currently Amended) The method ~~for detecting superantigen activity as claimed in claim 1, characterized in that:~~wherein:

(i) blood mononucleated cells are sampled, said cells originating from patients suffering from ~~an autoimmune disease or from patients suspected of having a risk of developing an autoimmune disease~~, multiple sclerosis and from healthy individuals,

(ii) said blood mononucleated cells originating from patients or from healthy individuals are brought into contact with a polypeptide or a recombinant protein, as identified in SEQ ID ~~No.~~NO: 2, or a fragment of said polypeptide, said fragment being at least six amino acids in length, and

(iii) said expansion and, optionally, co-expansion, or said loss and, optionally, co-decrease, using the blood mononucleated cells of step (i) are detected.

39. (Currently Amended) The method as claimed in claim 38, ~~characterized in that~~wherein a polypeptide comprising at least one or more fragment(s) of the env protein of MSRV-1 identified by SEQ ID ~~No.~~NO: 2, said fragment being at least ~~6~~eight amino acids in length, is used.

40. (Currently Amended) The method as claimed in claim 37, ~~characterized in that~~wherein said polypeptide is encoded by a nucleic acid comprising at least one or more fragment(s) of the RNA or of the DNA of the *env* gene of MSRV-1, identified by SEQ ID ~~No.~~NO: 1, said fragment being at least 18 nucleotides in length, or a vector comprising said nucleic acid.

41-77. (Canceled)

78. (New) The method as claimed in claim 1, wherein to calculate said amount of expansion or loss, the detected amount is compared to an amount of lymphocytes bearing a V β 16 and/or V β 17 in a biological sample of at least one healthy individual.

79. (New) The method as claimed in claim 4, wherein a co-expansion of lymphocytes bearing at least one of V β 3 and V β 12 is demonstrated.

80. (New) The method as claimed in claim 5, wherein a co-decrease of lymphocytes bearing at least one of V β 7, V β 14 and V β 17 is demonstrated.

81. (New) The method as claimed in claim 80, wherein a co-decrease of lymphocytes bearing at least one of V β 7 and V β 17 is demonstrated.

82. (New) The method as claimed in claim 7, wherein said established cell line is the PLI-2 cell line deposited at the ECACC on July 22, 1992, under the number 92072201, or the LM7PC cell line deposited at the ECACC on January 8, 1993, under the number 93010817, in accordance with the provisions of the Budapest Treaty.

83. (New) The method as claimed in claim 7, wherein said series of cultures comprise at least three cultures.

84. (New) The method as claimed in claim 9, wherein said established cell line is the PLI-2 cell line deposited at the ECACC on July 22, 1992, under the number 92072201, or the LM7PC cell line deposited at the ECACC on January 8, 1993, under the number 93010817, in accordance with the provisions of the Budapest Treaty.

85. (New) The method as claimed in claim 9, wherein said expansion and, optionally, co-expansion is demonstrated using ligands, each ligand being specific for a determinant chosen from V β 16, V β 2, V β 3, V β 7, V β 8, V β 12, V β 14, V β 17 and V β 22, and in that said loss and, optionally, co-decrease is demonstrated using ligands, each ligand being specific for a determinant chosen from V β 16, V β 2, V β 3, V β 7, V β 8, V β 12, V β 14, V β 17 and V β 22.

86. (New) The method as claimed in claim 85, wherein said expansion and, optionally, co-expansion is demonstrated using ligands, each ligand being specific for a determinant chosen from V β 16, V β 3 and V β 12.

87. (New) The method as claimed in claim 85, wherein said loss and, optionally, co-decrease is demonstrated using ligands, each ligand being specific for a determinant chosen from V β 16, V β 7, V β 14 and V β 17.

88. (New) The method as claimed in claim 10, wherein said expansion and, optionally, co-expansion is demonstrated using ligands, each ligand being specific for a determinant chosen from V β 16, V β 3 and V β 12.

89. (New) The method as claimed in claim 10, wherein said loss and, optionally, co-decrease is demonstrated using ligands, each ligand being specific for a determinant chosen from V β 16, V β 7, V β 14 and V β 17.

90. (New) The method as claimed in claim 11, wherein the antibody is a monoclonal antibody.

91. (New) The method as claimed in claim 85, wherein the ligand is an antibody or antibody fragment.

92. (New) The method as claimed in claim 91, wherein said antibody is a monoclonal antibody.

93. (New) The method as claimed in claim 9, wherein, in order to demonstrate said expansion and, optionally, co-expansion or said loss and, optionally, co-decrease, the following is carried out:

(i) extraction of the total RNAs from the blood mononucleated cells which have been placed together with MS culture supernatant or a fraction of MS culture supernatant and together with control culture supernatant or a fraction of control culture supernatant,

(ii) reverse transcription of said RNAs,

(iii) amplification specific for each V β family using a given pair of primers,

(iv) labeling of the amplification products obtained, with any suitable label,

(v) electrophoresis of said amplification products and analysis of the electrophoretic profiles obtained, using a suitable detector.

94. (New) The method as claimed in claim 93, wherein the blood mononucleated cells originating from patients suffering MS are chosen from lymphocytes.

95. (New) The method as claimed in claim 32, wherein to calculate said amount of expansion or loss, the detected amount is compared to an amount of lymphocytes bearing V β 7 in a biological sample of at least one healthy individual.

96. (New) The method as claimed in claim 33, wherein said established cell line is the PLI-2 cell line deposited at the ECACC on July 22, 1992, under the number 92072201, or the LM7PC cell line deposited at the ECACC on January 8, 1993, under the number 93010817, in accordance with the provisions of the Budapest Treaty.

97. (New) The method as claimed in claim 35, wherein said established cell line is the PLI-2 cell line deposited at the ECACC on July 22, 1992, under the number 92072201, or the LM7PC cell line deposited at the ECACC on January 8, 1993, under the number 93010817, in accordance with the provisions of the Budapest Treaty.

98. (New) The method as claimed in claim 36, wherein the ligand is an antibody or an antibody fragment.

99. (New) The method as claimed in claim 98, wherein said antibody is a monoclonal antibody.

100. (New) The method as claimed in claim 36, wherein, in order to demonstrate said expansion and, optionally, co-expansion or said loss and, optionally, co-decrease, the following is carried out:

(i) extraction of the total RNAs from the blood mononucleated cells which have been placed together with MS culture supernatant or a fraction of MS culture supernatant and together with control culture supernatant or a fraction of control culture supernatant,

(ii) reverse transcription of said RNAs,

(iii) amplification specific for each V β family using a given pair of primers,

(iv) labeling of the amplification products obtained, with any suitable label,

(v) electrophoresis of said amplification products and analysis of the electrophoretic profiles obtained, using a suitable detector.

101. (New) The method as claimed in claim 37, wherein said polypeptide is a recombinant protein.

102. (New) The method as claimed in claim 37, wherein said series of cultures comprises at least three cultures.

103. (New) A method for detecting multiple sclerosis or a condition associated with multiple sclerosis, in a biological sample from a patient having or suspected of having multiple sclerosis or having a risk for developing multiple sclerosis, said method comprising:

detecting an amount of lymphocytes bearing a V β 16 and/or V β 17 determinant in said biological sample; and

calculating an amount of expansion or loss of lymphocytes bearing a V β 16 and/or V β 17 determinant based on said detected amount,

wherein a majority expansion of lymphocytes bearing a V β 16 and/or V β 17 determinant or a majority loss of lymphocytes bearing a V β 16 and/or V β 17 determinant is indicative of multiple sclerosis or a condition associated with multiple sclerosis.

104. (New) A method for detecting multiple sclerosis or a condition associated with multiple sclerosis, in a biological sample from a patient having or suspected of having multiple sclerosis or having a risk for developing multiple sclerosis, said method comprising:

detecting an amount of lymphocytes bearing a V β 7 determinant in said biological sample; and

calculating an amount of expansion or loss of lymphocytes bearing a V β 7 determinant based on said detected amount,

wherein a majority expansion of lymphocytes bearing a V β 7 determinant or a majority loss of lymphocytes bearing a V β 7 determinant is indicative of multiple sclerosis or a condition associated with multiple sclerosis.